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Note

An efficient conversion of 2′-hydroxychalcones into flavanones : Use of tetra-*n*-butylammonium iodide

Deepika Dhawan & S K Grover*

Department of Chemistry, University of Delhi, Delhi 110 007, India

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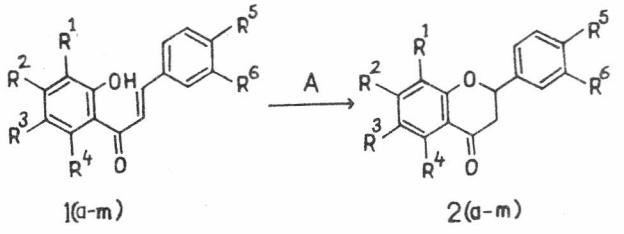
2′-Hydroxychalcones **1** possessing different substitution patterns in rings A and B, have been found to undergo efficient isomerization to the corresponding flavanones **2** when heated in ethanol with hydrochloric acid and tetra-*n*-butylammonium iodide.

Flavanones form a large and important group of naturally occurring polyphenolics. They are important intermediates for the synthesis of biologically active flavones[1,2] and isoflavones[3]. Isomerizations of chalcones to flavanones is usually carried out in the presence of an acid or a base[4-9]. An efficient isomerization of 2′-hydroxychalcones to the corresponding flavanones has been a subject of our interest since these were required for a study of the mechanism of the unusual oxidation reaction of isoflavanones to isoflavones when treated with chlorotrimethylsilane in acetic anhydride, reported earlier from our laboratories[10].

The various methods[4-9] for isomerization of 2′-hydroxychalcones to flavanones on re-investigation have been found to give the desired compound in very poor yield, particularly when carried out on a semi-micro scale. It is important to mention here that the recent methods for the above isomerization using trifluoroacetic acid[11] and hydroxylamine hydrochloride/sodium hydroxide[12] have failed to work in our hands and the chalcones were recovered unchanged. The functional use of hydroxylamine hydrochloride in a highly basic medium[12] is difficult to explain. Correspondence with the authors[11,12] followed by repetition of their work under the conditions suggested did not yield any fruitful results or improvement.

Of the various methods available in literature, reproducible results were obtained by refluxing 2′-hydroxy-4′-methoxychalcone (a typical example) in ethanolic hydrochloric acid[8] when the corresponding flavanone was obtained in 20% yield; with ethanolic sulphuric acid[9] the yield was



A : EtOH – HCl , $(n\text{-}C_4H_9)_4N^+Cl^-$

10%. Better yield of the isomerised product in the presence of hydrochloric acid could be attributed to the behaviour of chloride ion as a better counter ion. It was, therefore, considered worthwhile to study the reaction in the presence of iodide ion. Addition of sodium or potassium iodide to the reaction mixture did not lead to any improvement.

However, 2′-hydroxychalcones **1** underwent efficient isomerization to the corresponding flavanones **2** (Table I) when refluxed with tetra-*n*-butylammonium iodide in ethanol-hydrochloric acid. Even in this case complete conversion to flavanones did not take place. TLC study of the reaction mixture showed it to be a mixture of the starting chalcone and the corresponding flavanone, in which the latter was present as the major product. When the above isomerization was attempted in ethanolic sulphuric acid containing tetra-*n*-butylammonium iodide, the yields of the desired products were found to be much lower than those obtained by ethanolic hydrochloric acid tetra-*n*-butylammonium iodide procedure. Addition of tetra-*n*-butylammonium hydrogn sulphate or triethyl(benzyl)ammonium chloride did not prove as useful.

The routine method of separation of the mixture of chalcone and flavanone by utilizing preferential solubility of chalcones in ether has been modified by carrying out the separation using column chromatography over basic alumina when flavanones eluted preferentially giving the desired compounds in a state of high purity.

Experimental Section

General procedure. A solution of substituted 2′-hydroxychalcone (**1a-m**, 0.10 g) in ethanol (7.50 mL) and hydrochloric acid (1.85 mL) con-

Table I — Melting points and yields of flavanones **2**

Compd	R^1	R^2	R^3	R^4	R^5	R^6	m.p. °C	lit.m.p. °C	Yield (%)
2a	H	H	H	H	H	H	75-76	75-76[13]	56
2b	H	H	H	H	OCH_3	H	96	97[13]	52
2c	H	H	H	H	OCH_3	OCH_3	126	126[14]	53
2d	H	OCH_3	H	H	H	H	90	89[15]	65
2e	H	OCH_3	H	H	OCH_3	H	94	94-95[16]	58
2f	H	OCH_3	H	H	OCH_3	OCH_3	120	120-21[17]	50
2g	H	OCH_3	H	OCH_3	H	H	141	140[15]	66
2h	H	OCH_3	H	OCH_3	OCH_3	H	123	123[18]	63
2i	H	OCH_3	H	OCH_3	OCH_3	OCH_3	160	161[19]	67
2j	OCH_3	OCH_3	H	H	H	H	119	120[20]	75
2k	OCH_3	OCH_3	H	H	OCH_3	H	115	115[21]	78
2l	OCH_3	OCH_3	H	H	OCH_3	OCH_3	145	143.5-44[21]	75
2m	H	H	CH_3	H	OCH_3	H	109	110[12]	85

taining tetra-*n*-butylammonium iodide (0.05 g) was refluxed for 96 hr (till no further change in composition was observed on TLC). The reaction mixture was concentrated to half its volume under reduced pressure and treated with aqueous sodium thiosulphate (10%, 10 mL). This mixture was extracted with ether (2 × 15 mL) and ether layer extracted successively with aqueous sodium bicarbonate (8%, 15 mL) and water (2 × 20 mL). The residue, obtained after removal of the solvent, was kept *in vacuo* over phosphorus pentoxide for 24 hr. This residue, which was a mixture of flavanone and the starting chalcone, was purified by column chromatography over basic alumina using benzene as eluent. Benzene eluate on concentration and treatment with light petroleum gave the corresponding flavanone (**2a-m**) in 50-85% yield (cf. Table I).

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